

Supplementary Video Legends

Video 1: Parasternal long-axis view of family 1 proband showing posterior leaflet prolapse and dilated left-heart chambers.

Video 2: Zoomed view of thickened, prolapsing leaflet in family 1 proband.

Video 3: Doppler color flow mapping of family proband 1 showing severe MR, increasing with prolapse throughout systole.

Video 4: High-speed video of wild type (control injected) *D. rerio* heart at 72 hours post-fertilization (hpf). At this stage the heart has looped and blood flow is unidirectional from the atrium (upper right) to the ventricle, and a constriction has formed at the junction between the atrium and ventricle. No regurgitation is evident.

Video 5: High-speed video of *dchs1b* morphant *D. rerio* heart at 72 hpf. Hearts of *dchs1b* morphants fail to loop properly and there is regurgitation of blood from the ventricle (lower right) into the atrium (upper left). Concomitant with this phenotype, there is reduced constriction of the AV canal.

Video 6: Parasternal long axis view of adult (9-month old) *Dchs1^{+/+}* heart showing normal mitral valve opening and closing.

Video 7: Parasternal long-axis view of adult (9-month old) *Dchs1^{+/-}* heart showing anterior and posterior leaflet thickening and posterior leaflet prolapse. Prolapse is most easily observed at frames: 149, 188, and 300

Video 8: Movie of 3D reconstructions of *Dchs1*^{+/+} 9-month old posterior leaflet obtained from micro-MRI slices. Following this movie is an additional movie of 3D reconstructions of *Dchs1*^{+/-} 9-month old posterior leaflet also obtained from micro-MRI slices.

Video 9: Movie of AMIRA 3D reconstruction of *Dchs1*^{+/+}, *Dchs1*^{+/-}, and *Dchs1*^{-/-} E17.5 mitral leaflets. Respective 3D reconstructions are shown sequentially during the movie. Green=Anterior Leaflet, Blue =Posterior Leaflet.

Video 10: AMIRA 3D reconstruction of EPDC lineage trace in *Dchs1*^{+/+} and *Dchs1*^{+/-} PO posterior mitral leaflets. Respective 3D reconstructions are shown sequentially during the movie. Green=EPDC, Blue =non-EPDCs